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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/661,977

09/11/2003

Benjamin L. Viglianti

180/157/2/2

8988

25297

7590

10/23/2006

JENKINS, WILSON, TAYLOR & HUNT, P. A.

3100 TOWER BLVD

SUITE 1200

DURHAM, NC 27707

EXAMINER

CHAO, ELMER M

ART UNIT

PAPER NUMBER

3737

DATE MAILED: 10/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

NIT

Office Action Summary	Application No. 10/661,977	Applicant(s) VIGLIANTI ET AL.	
	Examiner Elmer Chao	Art Unit 3737	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-40 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-40 is/are rejected.
- 7) ☒ Claim(s) 36 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 September 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>See Continuation Sheet</u> . | 6) <input checked="" type="checkbox"/> Other: <u>WO9844910</u> . |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :6/30/2005 & 7/19/2004 & 12/29/2003.

DETAILED ACTION

Claim Objections

Claim 36 is objected to because of the following informalities: The sentence segment "...comprises. a formulation..." in the first sentence is not supposed to contain a period between the words "comprises" and "a". Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 6, 7, 19, 20, and 25-28 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Lang (WO 98/44910). Lang '910 discloses a method of monitoring the drug delivery to a tumor (pg 5, L3-5), the method comprising:

- (a) administering to a subject a non-sensitive liposome composition comprising:
 - (i) a contrast agent (pg 5, L7-8), wherein the contrast agent comprises an element selected from the group consisting of Gd (pg 3, L7 & 11);
 - (ii) a therapeutic agent (pg 5, L14-15), wherein the therapeutic agent is a chemotherapeutic agent (pg 7, L8-16); and
 - (iii) a non-sensitive liposome encapsulating the contrast agent and the compound of interest (pg 5, L9-15); and

(b) monitoring the accumulation of the compound of interest at the tumor site by magnetic resonance imaging (pg 5, L16; pg 5, L3-5; By monitoring via MRI imaging, the operator would be able to visually examine differences in pixel densities.).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 8, 12, 13, 15-18, 22, 23, 29-31, 33, and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fenn (U.S. 5,810,888). Lang '910 discloses all of the limitations as discussed above. Lang '910 does not disclose the use of a thermo-sensitive liposome for drug delivery. Fenn '888 teaches the use of a thermo-sensitive liposome for drug delivery by transmitting electromagnetic radiation to the site of interest wherein the liposome contains chemotherapy agents (C17, Claim 15-17, the thermal breakdown of thermo-sensitive liposomes would release the contrast agent disclosed by Lang '910). Fenn '888 also discloses the possibility of using medical imaging modalities such as Magnetic Resonance Imaging to detected the temperature of the site while heating (C9, L21-27). It would have been obvious to a person of ordinary skill in the art to modify Lang '910 to include the use of a thermo-sensitive liposome in the method of

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drug delivery and monitoring as evidenced by Fenn '888. Such a modification would increase the concentration of a drug within the tumor during drug delivery (C2, L19-22).

Claims 2, 3, 9-11, 35, and 37-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lang '910 in view of Fenn '888, and further in view of Unger (U.S. 5,149,319). Lang '910 and Fenn '888 disclose all of the limitations as discussed above. Lang '910 does not disclose the use of ultrasound to heat the tumor site. However, Unger '319 teaches the use of ultrasound to heat the tumor site (C1, L54-58). It would have been obvious to a person of ordinary skill in the art at the time of the invention to modify Lang '910 to include the use of ultrasound to heat the tumor site as evidenced by Unger '319. Such a modification would be advantageous by causing tumor cells to die and eventually destroying the tumor (C1, L24-31, by heating the site of interest, blood flow is also increased).

Claims 14, 24, 32, and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lang '910 in view of Fenn '888, further in view of Unger '319, and further in view of Unger et al. (U.S. 5,542,935). All the limitations are disclosed as discussed above. None of the references described except for Unger '935 discloses a particular formulation of a thermo-sensitive liposome. Unger '935 discloses many different formulations of liposomes, including DPPC-PEG (C19, L24-39). It would have been obvious to a person of ordinary skill in the art to use a thermo-sensitive liposome comprising a formulation of PEG and DPPC. Liposomes are often linked to polymers of polyethylene glycol in order to achieve greater stability (C19, L24-27).

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Dipalmitoylphosphatidylcholine is used in thermo-sensitive liposomes for their ability to rupture on application and for their stability (C19, L36-39).

Claims 5 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lang '910 in view of Gamble et al. (U.S. 4,728,575). Lang '910 discloses all of the limitations as discussed above. Lang '910 does not describe a liposome wherein the liposome comprises DSPC/Cholesterol. However, Gamble '575 teaches the use of a liposome comprising DSPC/Cholesterol (C4, L14). It would have been obvious to a person of ordinary skill in the art at the time of the invention to modify Lang '910 to use a lipid formulation of DSPC/Cholesterol as evidenced by Gamble '575. Such a modification would be advantageous in MRI contrast agent enhancement by promoting vesicle stability of the liposome that encapsulates the contrast agent (abstract).

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Grinstaff et al. (U.S. 5,665,383); Kirpotin et al. (U.S. 5,411,730); Gamble et al. (U.S. 6,468,505); Schneider et al. (U.S. 6,258,378 B1); Unger et al. (U.S. 6,231,834 B1); Needham (U.S. 6,200,598); Lang et al. (U.S. 6,468,505).

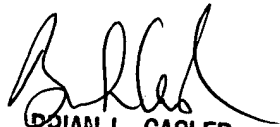
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elmer Chao whose telephone number is (571)272-0674. The examiner can normally be reached on 9am-4pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Casler can be reached on (571)272-4956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

EC
10/10/2006


BRIAN L. CASLER
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 3700